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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,332	07/17/2003	John C. Voyta	9550-015-27	8651

23552 7590 03/06/2007
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EXAMINER	
FOSTER, CHRISTINE E	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)
	10/620,332	VOYTA ET AL.
	Examiner	Art Unit
	Christine Foster	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 17 January 2007.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,3-5,7-10,13,16-19,21-32 and 34-45 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,3-5,7-10,13,16-19,21-32 and 34-45 is/are rejected.

7)☒ Claim(s) 39 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment, filed 1/17/2007, is acknowledged and has been entered. Claims 6, 14-15, and 33 were canceled by the amendment. Claims 1, 13, 19, 24, 26, 30, 37, 40, 42 and 44 were amended. Claims 1, 3-5, 7-10, 13, 16-19, 21-32, and 34-45 are currently pending and under examination.

Objections/Rejections Withdrawn

2. The objections to claims 6, 33, 40 and 42 have been withdrawn in response to Applicant's amendments and in light of the cancellation of claims 6 and 33.

3. The rejection of claim 1 under 112, 2nd paragraph as omitting essential structural relationship is withdrawn in response to Applicant's amendment to recite that the probes are immobilized on the support.

4. The rejections of claims 13, 19, 26, 30-31, 42-44 under 112, 2nd paragraph for lack of antecedent basis are withdrawn in view of the amendments.

5. The rejections of claims 1, 3-5, 9, 13-15, 21, 29, 31-32, and 44 under 35 U.S.C. 103(a) as being unpatentable over Cheek et al. in view of in view of Akhavan-Tafti (US Patent No. 6,068,979) have been withdrawn in response to Applicant's amendments to claim 1 to recite that the solid support, rather than simply the surface layer of the solid support, is two-dimensional. Similarly, the rejections of dependent claims 7-8, 16-19, 22-28, 30, 34-43, and 45 as being unpatentable over Cheek et al. in view of Akhavan-Tafti and further in view of various references as set forth in the previous Office action have also been withdrawn for this reason.

However, should the claims be amended to address the new grounds of rejection under 35 USC 112, 1st paragraph (new matter) set forth below, the rejections over the references may be reconsidered.

Claim Objections

6. Claim 39 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 39 recites that the first chemiluminescent substrate is a 1,2-dioxetane substrate and that the second chemiluminescent substrate is selected from the group consisting of an acridan ester, an acridan thioester, an enol phosphate, an acridan enol phosphate, and a luminol substrate. However, independent claim 1 recites that the both the first and the second chemiluminescent substrates are 1,2-dioxetanes. As a result, claim 39 appears to broaden, rather than further limit, the parent claim since it apparently requires that the second substrate be something other than a 1,2-dioxetane, which is a requirement of the parent claim.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 3-5, 7-10, 13, 16-19, 21-32, and 34-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

9. Claim 1 as amended recites a "two-dimensional solid support having a surface layer". The claim previously referred to a "two-dimensional solid support surface layer". Applicant's reply states that support for the amendments may be found at p. 14, lines 11-12, which discloses:

> The solid support surface may be two-dimensional (i.e., substantially planar). Alternatively, the support surface may be non-planar.

However, support could not be found in the above passage for the currently claimed limitation that the *support* is two-dimensional, since the specification refers only to the *surface* of the support being two-dimensional. By contrast, the claim now conveys that the *support,* rather than the *surface* of the support, is two-dimensional. As a result, the amendments to the claim such that "two-dimensional" now refers to the *solid support* itself and not to the *surface layer* of the solid support represent new matter because such limitations are not disclosed in the specification.

10. Claim 1 as amended recites that the first and second chemiluminescent substrates are contacted with the surface layer in the presence of a composition comprising an **onium polymer** or an onium copolymer chemiluminescent quantum yield enhancing material. Support could not be found in the specification for the currently claimed method employing a composition comprising an *onium polymer*.

Claim 40 previously recited that "the chemiluminescent quantum yield enhancing material is an onium polymer selected from the group consisting of poly(vinylbenzylammonium salts), poly(vinylbenzylphosphonium salts), and poly(vinylbenzylsulfonium salts)".

The currently amended claim represents a departure from the specification and claims as originally filed because although original claim 40 refers to an "onium polymer", this was in the context of a Markush group of three specific types of onium polymers. These three types of onium polymers are also disclosed in the specification at p. 5, lines 20-24; however they are not specifically identified as "onium polymers" therein. The specification does not introduce the concept of the genus of "onium polymers".

Claim 1 as amended is broader in scope, being not limited to the three disclosed species of onium polymers. No generic support could be found in the specification for compositions comprising (all) onium polymers as the chemiluminescent quantum yield enhancing material. The generic disclosure of "a composition comprising a quantum yield enhancing material" and of the three species (poly(vinylbenzylammonium salts), poly(vinylbenzylphosphonium salts), and poly(vinylbenzylsulfonium salts)) does not support the currently claimed subgenus drawn to a "composition comprising an onium polymer".

The amendments therefore represent new matter as they effectively create a new subgenus. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05. One skilled in the art would not envisage possession of the genus of "onium polymers" according to the instantly claimed methods given that such a genus is never introduced in the specification.

11. Claims 24 and 30 as amended recite that fluorescent labels are attached directly or indirectly to a probe. Applicant's reply indicates that support may be found at p. 7, lines 15+ (see reply, p. 11, the first paragraph). However, support could not be found where indicated since the passage mentioned by Applicant refers only to attachment of *enzyme conjugates* to probes and not to attachment of *fluorescent labels* to probes. Support could not be found in the specification for the instantly claimed methods wherein fluorescent labels are attached directly or indirectly to a probe. There is no generic disclosure in the specification of "fluorescent labels attached directly or indirectly to a probe" as currently claimed.

The specification discloses that the support surface may comprise fluorescent labels (p. 9, lines 11-18), but this passage does not provide support for fluorescent labels attached "directly or indirectly" to probes since it does not detail in what way the fluorescent labels are attached to the support.

The specification also discloses that control targets can be labeled with fluorescent labels (see p. 9, lines 4-10). Such control targets would then presumably bind to control probes on the support surface.

Similarly, the specification similarly discloses that control labels (which include fluorescent labels as disclosed at p. 16, lines 9-11) can be attached "directly to a probe for a target molecule or via attachment to a different molecule" (p. 15, line 17 to p. 16, line 11). The specification also discloses in this section that a control label can be attached to a control target capable of binding to a control probe.

Such scenarios, in which fluorescent labels are indirectly attached to *control targets* that are capable of binding to *control probes*, may at best be considered to represent a species reading

on the currently claimed genus of fluorescent labels "indirectly" attached to probes. However, the instant claims do not recite that the fluorescent labels are indirectly attached to *control targets* that then bind to *control probes*. Similarly, in the case of fluorescent labels being "directly" attached to a probe as claimed, the specification discloses only direct attachment of control labels to a probe for a target molecule (p. 15, line 23 to p. 16, line 2). The claims do not recite the accompanying limitations that the fluorescent label is a *control label*, or that the probe is a probe for a *target molecule*. As a result, the scope of what is claimed is broader than the disclosure.

Applicant is effectively claiming a subgenus not supported by the specification as filed. The disclosure of a specific example of "direct" attachment (control labels attached directly to probes for a target molecule) does not support the subgenus of fluorescent labels attached directly to probes as claimed. Likewise, the disclosure an example of "indirect" attachment (control probes attached to control targets that are capable of binding to a control probe) does not support the subgenus of fluorescent labels indirectly attached to a probe. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

12. Claim 13 as amended now recites that the surface layer is contacted with a sample comprising first target molecules labeled with a first label and contacted with a sample comprising second target molecules labeled with a second label (see lines 1-5 of the claim). The claim previously referred to a <u>single sample</u> comprising the first and second target molecules. No support could be found for the currently claimed method in which two samples are contacted with the surface layer, where the first sample comprises the first target molecules and the second

sample comprises the second target molecules. The specification at p. 12, lines 14-18 also refers to a single sample that comprises both the first and second target molecules.

13. Claim 37 as amended recites the further step of contacting the surface layer with a composition comprising the first and second enzyme conjugates. The claim has been amended so that it now depends from claim 13. The claim previously depended from claim 15, which referred to indirect labeling of the target molecules with moieties capable of binding to enzyme conjugates.

However, in the currently amended claim 13, the target molecules may be either directly (lines 6-8) or indirectly (lines 9-11) labeled with the first and second enzymes. As a result, the scope of dependent claim 37 has changed, such that the additional step recited could be performed in situations where the target molecules are *directly labeled* with enzymes. No support could be found for such a method in which the enzyme conjugates (target molecules directly labeled with enzymes) are contacted with the surface layer, followed by an additional step in which a composition comprising the enzyme conjugates are apparently contacted again with the surface layer (see also the rejection under 112, 2nd paragraph below).

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 13, 16-19, 29-31, and 37-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

16. Claim 13 recites that the surface layer of the solid support is contacted with a sample that comprises the first and second target molecules. The first and second target molecules may be (directly) labeled with the first and second enzymes to form the first and second enzyme conjugates, respectively (see lines 6-8 of the claim). The claim (and the claims that depend from them) therefore appears to describe a step in which the first and second enzyme conjugates become bound to the solid support. However, the claims depend from claim 1, which recites that the first and second enzyme conjugates are already bound to the surface layer. It is unclear how the enzyme conjugates may be contacted with the surface layer when they are already bound to the surface layer.

17. Claim 37 is also indefinite because it refers to contacting the surface layer with a composition comprising the first and second enzyme conjugates. The claim has been amended so that it now depends from claim 13. The claim previously depended from claim 15, which referred to indirect labeling of the target molecules with enzymes. In the currently amended claim 13, however, the target molecules may be either directly (lines 6-8) or indirectly (lines 9-11) labeled with the first and second enzymes. The claim is indefinite because in the case in which the target molecules are already directly labeled with the first and second enzymes to form the first and second enzyme conjugates (lines 6-8 of claim 13), it is unclear how the method could further include the step of contacting the surface with the first and second enzyme conjugates since the first and second enzyme conjugates have already been contacted with the surface. Furthermore, as also discussed above with respect to claim 13, it is also unclear how the surface layer may be contacted with a composition comprising the enzyme conjugates when they are already bound to the surface layer.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 1, 3-5, 7, 9, 13, 21, 25, 27-29, 31-32, 34, 40-41, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti (US Patent No. 6,068,979) in view of Akhavan-Tafti et al. ("Chemiluminescent Detection of DNA in Low- and Medium-Density Arrays," *Clinical Chemistry* **44**:2065-2066 (1998)) and Bronstein et al. (US Patent No. 4,931,223).

Akhavan-Tafti '979 teaches a method of detecting chemiluminescent emissions on a solid support substantially as claimed. The method includes the steps of contacting a surface layer of the solid support with a composition comprising a first chemiluminescent substrate capable of being activated by a first enzyme to produce a first chemiluminescent signal, detecting the first

chemiluminescent signal on the surface layer of the solid support, contacting the surface layer of the solid support with a composition comprising a second chemiluminescent substrate capable of being activated by a second enzyme to produce a second chemiluminescent signal, and detecting the second chemiluminescent signal on the surface layer of the solid support (see in particular column 6, lines 17-24, 41-45 and 60-67; and column 7, lines 1-46; column 10, lines 59-67; and column 11, lines 1-44).

Akhavan-Tafti '979 further teaches 1,2-dioxetane chemiluminescent substrates as the second chemiluminescent substrate (see column 8, line 65 to column 10, line 58, and especially the chemical diagrams at the top of columns 9 and 10, which depict 1,2-substituted dioxetane chemiluminescent substrates). The reference further teaches the use of chemiluminescent quantum yield enhancing materials, which may be onium polymers (column 10, lines 24-47) including poly(vinylbenzylamm*onium*) salts or polymeric phosph*onium* salts. These onium polymers may be included in the 1,2-dioxetane chemiluminescent substrate compositions (see column 9, lines 46-52; column 10, lines 15-47 and US Patent 5,45,347, which was incorporated by reference). Akhavan-Tafti '979 teaches that when such enhancers are included with the second (dioxetane) chemiluminescent substrate as part of a detection reagent, they have the effect of improving the signal to background ratio of enzymatically-produced chemiluminescence (column 10).

Akhavan-Tafti '979 differs from the claimed invention in that it fails to specifically teach a method wherein a plurality of probes is disposed on the surface layer at a density of at least 50 or at least 100 discrete areas per cm^2. The reference also fails to specifically teach that both the first and second chemiluminescent substrates are 1,2-dioxetane substrates.

Akhavan-Tafti et al. teach chemiluminescent detection of DNA in low- and medium-density arrays of 100 spots per cm^2 (p. 2065, right column, paragraph 4). Akhavan-Tafti et al. further teach that such arrays are useful in high-throughput analysis of gene mutations and gene expression (p. 2065, right column, paragraph 1) and can be combined with chemiluminescent analysis with no expensive instrumentation (p. 2066, right column, last paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ the method of sequentially detecting chemiluminescent emissions of Akhavan-Tafti '979 using arrays with a plurality of probes disposed on a surface layer at a density of at least 50 or 100 discrete areas per cm^2 as taught by Akhavan-Tafti et al. in order to allow high-throughput analysis of gene mutations and expression. One would have had reasonable expectation of success in combining the array of Akhavan-Tafti et al. with the sequential chemiluminescent detection method of Akhavan-Tafti '979 because Akhavan-Tafti et al. established that chemiluminescent detection was feasible with array formats. One would also have a reasonable expectation of success because the sequential detection method of Akhavan-Tafti '979 involves detection of chemiluminescent emissions on a nylon membrane, which is the same material used as the solid support in Akhavan-Tafti '979.

Bronstein et al. teach methods for detecting chemiluminescent emissions using two or more 1,2-dioxetane substrates, which may be used in quantifying several analytes when each of the 1,2-dioxetanes emits light of a different wavelength (column 2, line 42 to column 3, line 3; 6, lines 44-47; column 7, lines 5-19; column 8, lines 1-29 in particular).

Therefore, it would have been further obvious to one of ordinary skill in the art at the time of the invention to employ two 1,2-dioxetane substrates as taught by Bronstein et al. in the

method of Akhavan-Tafti '979 and Akhavan-Tafti et al. for the purpose of producing chemiluminescent signals because Bronstein et al. teach that two or more 1,2-dioxetane substrates may be successfully used in a chemiluminescent detection assay for the quantification of two or more analytes, such as that of Akhavan-Tafti '979 and Akhavan-Tafti et al., in order to enable multichannel assays. One would have a reasonable expectation of success because Bronstein et al. teaches that two or more enzymatically-cleavable 1,2-dioxetane substrates can be used in either sequential or simultaneous detection methods, which is applicable to the sequential detection method of Akhavan-Tafti '979 (column 1, line 53 to column 2, line 19, and especially at column 2, line 11).

When using two 1,2-dioxetane substrates as taught by Bronstein et al., it would have also been further obvious to contact the surface layer with the substrate compositions in the presence of onium polymers such as poly(vinylbenzylammonium) salts since Akhavan-Tafti '979 teaches that such enhancer compounds, when included in 1,2-dioxetane substrate compositions, improve the signal/background ratio of chemiluminescence. Since such onium polymers are included together with the substrate to form the detection reagent, the chemiluminescent substrate would necessarily be contacted with the surface layer in the presence of the onium polymer.

With respect to claims 38, 31, and 40-41, Akhavan-Tafti '979 also discloses use of chemiluminescent quantum yield enhancing materials, which may be onium polymers (column 10, lines 24-47) including poly(vinylbenzylammonium) salts and which may be present in the chemiluminescent substrate composition (see column 9, lines 46-52; column 10, lines 15-47 and US Patent 5,45,347, which was incorporated by reference). Chemiluminescent substrates are employed as buffered compositions (column 9, lines 46-47; column 10, lines 42-45, and column

15, lines 1-8). Washing of the solid support may be performed prior to contacting with the first substrate composition (column 15, lines 48-51) or after the first detection step (column 13, lines 9-13). As such, when using two 1,2-dioxetane substrates as taught by Bronstein et al., it would have been obvious to employ the enhancers taught by Akhavan-Tafti '979 in order to enhance the chemiluminescent signal since Akhavan-Tafti '979 directs the skilled artisan to include such enhancers in 1,2-dioxetane substrate compositions.

With respect to claims 3-5, 7, 13, and 44, Akhavan-Tafti '979 teaches first and second enzyme conjugates that are bound directly to probes or are bound to first and second target molecules that are bound to probes (columns 15-16, Example 2; column 14, lines 29-33 and 60-67; column 4, lines 31-40; column 5, lines 18-24). Also disclosed are antidigoxigenin:enzyme conjugates wherein the corresponding target molecules are labeled with digoxigenin (columns 15-16, Example 2). The enzyme conjugates are added prior to the addition of the substrate compositions (see column 15, lines 40-45 for example).

With respect to claims 25 and 27, Akhavan-Tafti '979 teach a variety of first and second substrates, including Lumigen PS-3 and Lumi-Phos Plus, which have emission maxima of 430 and 470 nm, respectively. Because the instant specification and claims do not define what wavelengths or range of wavelengths constitute "approximately the same" emission maxima, the examiner has considered that the emission maxima of 430 and 470 nm also meet this limitation.

Therefore, it would have been clearly obvious to employ the substrates luminol and APS-5, which have "approximately" the same but different emission maxima as evidenced by Weimar et al. in the method of Cheek et al. and Akhavan-Tafti et al. since these are the specific substrates are taught in Cheek et al.

Akhavan-Tafti '979 also discloses contacting a support surface with a sample comprising first and second target molecules labeled with a first second label (e.g., lambda phage DNA labeled with biotin and SPPI marker DNA labeled with digoxigenin) prior to contacting the support surface with the substrate composition (columns 15-16, Example 2 in particular). With regard to claim 31, the surface layer may be washed after contact with the first target molecule and prior to contact with the first chemiluminescent substrate (see column 15, lines 48-51). Target molecules can include pools of target nucleic acids and mRNA for expression studies (column 14, lines 12-17) and may be quantified (column 1, lines 55-58).

With respect to claim 34, Bronstein et al. teach that β-galactosidase and alkaline phosphatase are examples of enzymes that may be used in methods for cleaving different cleavable dioxetane substituents using two or more different enzymes, and that use of these enzymes to cleave 1,2-dioxetane substrates that emit light of different wavelengths enables multichannel assays to be performed (column 7, lines 5-19; column 13, "Assay Procedure"; and claim 1 in particular). For example, alkaline phosphatase may be used to cleave a 1,2-dioxetane substrate to emit light at 480 nm, while beta-galactosidase may be used to cleave another 1,2-dioxetane substrate in order to emit light at 515 nm (column 7). As such, it would have been obvious to one ordinary skill in the art to employ β-galactosidase and alkaline phosphatase as the different enzymes for detecting different wavelengths released from two or more 1,2-dioxetane compounds when using the 1,2-dioxetane compounds of Bronstein et al. because such compounds are provided with groups cleavable by these enzymes. More generally, it would have been obvious to employ these known enzymes because they are known to be suitable for the purpose of cleaving 1,2-dioxetane substrates, as specifically taught in Bronstein et al.

21. Claims 16-19 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 in view of Akhavan-Tafti et al. and Bronstein et al., and further in view of Wang et al. (WO 01/73134 A2).

Akhavan-Tafti '979 and Akhavan-Tafti et al. are as discussed above, which fail to teach methods wherein the target molecules are pools of nucleic acids, comprise mRNA transcripts, cDNA or cRNA transcripts, or wherein the concentration of target nucleic acids is proportional to the expression level of genes. The references also fail to specifically teach cDNA target molecules labeled with digoxigenin. Akhavan-Tafti '979 does teach the digoxigenin-antidigoxigenin labeling system for mRNA; column 6, lines 25-34. However, the references fail to specifically teach a method wherein cDNA target molecules are labeled with digoxigenin.

Wang et al. teach ordered arrays of pools of target molecules (nucleic acids) on a solid support, where the mixtures reflect the expression profile of different cells or tissues (the abstract). Target molecules include mRNA or DNA derived from mRNA (such as cDNA), which can be used in microarray methods for analysis of gene expression in order to provide a relatively accurate indication of the level of expression of each gene in a cell (p. 24, lines 21-37 and p. 26, lines 24-33) Wang et al. also note that cDNA can be used in place of mRNA target samples because cDNA is more stable. Detecting of such targets can be used for mutation detection, genotyping, and DNA sequence analysis (p. 1, lines 10-15).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the method of Akhavan-Tafti '979 and Akhavan-Tafti in order to detect pools of nucleic acids (such as mRNA, cDNA or cRNA transcripts) in order to analyze gene expression. One would have

reasonable expectation of success because Wang et al. teach that such target molecules may be detected in microarray formats using chemiluminescent detection (p. 3, line 35 to p. 4, line 2).

22. Claims 22-24 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 in view of Akhavan-Tafti et al. and Bronstein et al., and further in view of Ferea et al. (US Patent 6,905,826 B2).

The references fail to specifically teach a method wherein control probes are located on the support surface, or wherein control probes are co-located in one or more of the same discrete areas as the plurality of probes.

Ferea et al. teach methods for detecting of target molecules in a sample using nucleic acid microarrays and in particular controls signals to be used in such methods. Such control signals allow for correction of irregularities in the shape, size, and intensity of microarray features (column 5, lines 49-52). Control signals additionally may be used to quantify the experimental signal (column 6, lines 16-19). Control oligonucleotide probes deposited on the array in the same discrete areas ("features") as the experimental probes can be used as hybridization controls (see column 6, lines 41-60; claim 1 and Figure 4 in particular). Control labels, which may include fluorescent labels, are used to confirm that the experimental probes are present and to help quantitate the experimental signal (column 6, lines 15-19 and claim 15). The relative amount of multiple experimental target sequences can be calculated by comparing the ratios of intensities of the experimental and control label signals. The control labels can be directly attached or conjugated to a subset of the experimental probes (column 6, lines 41-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include the control probes taught by Ferea et al. in the method of Akhavan-Tafti

'979 and Akhavan-Tafti et al. because Ferea et al. teach the benefit of control probes in determining whether hybridization is occurring in a microarray-format nucleic acid hybridization method and to help quantify the experimental signal. It would have been further obvious to include a fluorescent label as a control label and to compare the intensity of the signal from the fluorescent label to the experimental chemiluminescent signals because Ferea et al. teach that such control labels may be used to help quantify experimental signals in a microarray-format nucleic acid hybridization method using chemiluminescent and/or fluorescent detection. One would have a reasonable expectation of success because Ferea et al. teach that the control labels can used in conjunction with chemiluminescence labeling (see claim 17 in particular), which is the detection method of Akhavan-Tafti '979, Akhavan-Tafti, and Bronstein et al.

23. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 in view of Akhavan-Tafti et al. and Bronstein et al., and further in view of Gambini et al. (US Patent No. 6,518,068 B1).

The references fail to specifically teach a method wherein detection of the second chemiluminescent signal comprises filtering the emissions with a filter adapted to reduce the intensity of the first chemiluminescent signal relative to the intensity of the second.

Gambini et al. teach a detection workstation for analysis of luminescent signals that comprises a filter (or filters on a filter wheel) which permits the selection of different wavelength ranges, and which may be used to separate the emissions of different reagents emitting at different wavelengths. The workstation may be used in a method for detecting multiple luminescent signals emitting at different wavelengths (see the abstract and column 6, line 55 to column 7, line 13). Gambini et al. further teach that signals from multiple reagents are separated

using the filters, which are designed to maximize the sensitivity of the target reagent emission, while minimizing the sensitivity to other non-target reagent emission (column 13, line 60 to column 14, line 10).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the filter detection method taught by Gambini et al. in the method of Akhavan-Tafti '979 and Akhavan-Tafti et al. because Gambini et al. teach that such filters may be used to separate signals at different wavelengths by multiple reagents in a method for detection of multiple luminescent signals.

24. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 in view of Akhavan-Tafti et al. and Bronstein et al. as applied to claim 34 above, and further in view of Voyta et al. (US Patent No. 5,145,772).

The references fail to specifically teach that the composition comprising a chemiluminescent substrate capable of being activated by alkaline phosphatase comprises a 0.1M solution of aminomethylpropanol and 1 mM $MgCl_2$ at a pH of 9.5.

Voyta et al. teach a chemiluminescence detection method employing alkaline phosphatase as an enzyme label, wherein the enzyme is used in a solution containing 0.05M carbonate or Tris buffer solution and 1 mM $MgCl_2$ at pH=9.5 (column 11, lines 49-55 and column 13, lines 10-17). The above solution is used in order to dissolve enhancer substances, which stabilize chemiluminescent substrates and thereby increase the intensity of chemiluminescent emissions (see also column 2, lines 45-65 and Table 2).

Although Voyta et al. teach carbonate rather than sodium phosphate, it is well known in the art that these buffers may be interchanged in order to maintain a solution pH of 9.5. Further,

while the concentration of the buffer used by Voyta et al. differs, such a difference will generally not support patentability in most cases, constituting optimization of ranges within prior art conditions (see MPEP 2144.05).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ a solution comprising a buffer with a buffering capacity sufficient to maintain a pH of 9.5 in conjunction with 1 mM $MgCl_2$ in the method of Akhavan-Tafti '979 and Akhavan-Tafti in order to dissolve enhancer substances and thereby enhance the chemiluminescent signal. One would have a reasonable expectation of success because Voyta teaches that such a solution is effective in a chemiluminescence detection method employing alkaline phosphatase.

25. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 in view of Akhavan-Tafti et al. and Bronstein et al. as applied to claim 34 above, and further in view of Bobrow et al. (US Patent No. 5,196,306).

The references fail to specifically teach a method wherein the composition comprising a chemiluminescent substrate capable of being activated by beta-galactosidase is a 0.1M solution of sodium phosphate and 1 mM $MgCl_2$ at a pH of 7.0.

Bobrow et al. teach use of beta-galactosidase in a solution comprising 10 mM sodium phosphate, 1 mM $MgCl_2$ at pH 7.0 (column 17, paragraph 2). Beta-galactosidase stored in this solution was shown to be active (Figure 7).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ a substrate solution containing 0.1M solution of sodium phosphate and 1 mM $MgCl_2$ at a pH of 7.0 because Bobrow et al. teach that a solution comprising sodium

phosphate buffer and 1 mM $MgCl_2$ was an appropriate solution that would not destroy enzyme activity in an assay involving beta-galactosidase, such as that of Akhavan-Tafti '979 and Akhavan-Tafti et al. Further, while the concentration of the buffer used by Voyta et al. differs, such a difference will generally not support patentability in most cases, constituting optimization of ranges within prior art conditions (see MPEP 2144.05).

26. Claims 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 in view of Akhavan-Tafti et al. and Bronstein et al. as applied to claim 13 above, and further in view of Clothier (US Patent No. 6,852,503 B1). The references fail to specifically recite contacting the surface layer of the support with a composition comprising the first and second enzyme conjugates.

Clothier teaches a dual enzyme chemiluminescent substrate formulation for use in methods involving two enzymes. Clothier teaches combining the two chemiluminescent enzymes (horseradish peroxidase and alkaline phosphatase) together prior to contacting the enzymes with the well surface (column 6, lines 25-36).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the enzyme conjugates together in a single composition prior to contacting with the support surface in the method of Akhavan-Tafti '979, Akhavan-Tafti, and Bronstein et al. since Clothier teaches that enzymes for chemiluminescent substrates may be successfully combined together in methods for chemiluminescence detection involving two enzymes, such as that of Akhavan-Tafti '979, Akhavan-Tafti, and Bronstein et al.

With respect to claim 38, it is noted that Akhavan-Tafti '979 teaches binding pairs, including antigen-antibody and biotin-avidin or streptavidin. One member of a binding pair may

be attached to an enzyme form an enzyme conjugate, which is then capable of interacting with a target molecule labeled with the other member of the binding pair (column 4, lines 30-40 and column 5, lines 18-28). Specific examples of antigen-antibody binding pairs include antigoxigenin-digoxigenin, and antidigoxigenin:enzyme conjugates are disclosed (columns 15-16, Example 2).

27. Claims 8 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 and Akhavan-Tafti et al. and Bronstein et al. as applied to claim 1 above, and further in view of Bronstein et al. (US Patent No. 6,602,658 B1).

Akhavan-Tafti '979 and Akhavan-Tafti et al. fail to teach a method wherein the surface layer is contacted with the enhancing material prior to contacting with the first chemiluminescent substrate composition.

Bronstein et al. '658 teach a method of measuring gene activity using sequential chemiluminescent detection of signal from two or more chemiluminescent substrates, wherein chemiluminescent signal enhancers such as onium copolymers, polyvinylbenzyltrimethylammonium chloride or BSA may be added to increase the intensity of the chemiluminescent signals in aqueous medium (column 11, lines 29-61). Bronstein et al. '658 further teach that the enhancer molecule can be added at any point during the method (column 13, lines 39-52).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to provide the quantum yield enhancing material before contacting the surface layer with the first chemiluminescent substrate composition, because Bronstein et al. '658 teach that the enhancing material may be added at any point in a method of sequential detection of

chemiluminescent signals such as that of Akhavan-Tafti '979. It would have been further obvious to employ onium copolymers, as taught by Bronstein et al. in the method of Akhavan-Tafti '979 and Akhavan-Tafti et al. in order to enhance the chemiluminescent signal.

28. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 and Akhavan-Tafti et al. and Bronstein et al. as applied to claim 1 above, and further in view of Fodor et al. (US 6,309,822 B1).

Akhavan-Tafti '979 and Akhavan-Tafti et al. are as discussed above, which teach methods of detecting chemiluminescent emissions on solid supports having probe densities of 100 per cm2, but which fail to specifically teach densities of 1,000 areas per cm2.

Fodor et al. teach high density probe arrays, in which greater than about 400,000 different probes can be immobilized per cm2 (see in particular the abstract; column 2, lines 33-43; column 3, lines 18-48). The high-density probe arrays can be used to detect and quantify target nucleic acid sequences and/or to monitor the expression of a multiplicity of genes (column 33, lines 20-31; column 5, lines 34-36; column 2, lines 53-61). Fodor et al. teach that the high density probe arrays offer several advantages, including reduced intra- and inter-array variability, increased information content, and higher signal-to-noise ratio (see column 12 to column 15, line 60). In particular, Fodor et al. note that the arrays have advantages over blotted arrays (which is the technique used in Bronstein et al.), such as significantly higher hybridization efficiencies (column 14, line 61 to column 15, line 12).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the high density probe arrays of Fodor et al. as the solid support in the method of detecting chemiluminescent emissions of Akhavan-Tafti '979 and Akhavan-Tafti et al. in order to allow

for increased information content and massively parallel processing of hybridization data, reduction of assay variability, and/or to detect and quantify a multiplicity of genes with increased information content and sensitivity.

One would have a reasonable expectation of success in using the solid support of Fodor et al. in the method of detecting chemiluminescent emissions of Akhavan-Tafti '979 and Akhavan-Tafti et al. because Fodor et al. teach that the microarrays may be used in methods employing chemiluminescent detection (column 49, lines 5-12, column 82, lines 43-65) and also that enzyme labels may be used (column 20, lines 51-61). One would also have a reasonable expectation of success because Fodor et al. teach that the solid support may be a nylon membrane (column 95, lines 49-57), which is the same material used as the solid support by Akhavan-Tafti et al.

29. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 in view of Akhavan-Tafti et al. and Greene et al. (US Patent No. 5,137,804).

It is noted that claim 39 does not properly depend from claim 1 (see objection to the claim above), which recites that *both the first and second substrates are 1,2-dioxetanes*. For the purposes of examination, claim 39 was interpreted as being drawn to the use of a 1,2-dioxetane as the first substrate; however, the second substrate was assumed to be an acridan, enol phosphate, or luminol as the second substrate as recited in claim 39 rather than a 1,2-dioxetane as recited in claim 1.

Akhavan-Tafti '979 teaches a method of detecting chemiluminescent emissions on a solid support substantially as claimed. The method includes the steps of contacting a surface layer of the solid support with a composition comprising a first chemiluminescent substrate capable of

being activated by a first enzyme to produce a first chemiluminescent signal, detecting the first chemiluminescent signal on the surface layer of the solid support, contacting the surface layer of the solid support with a composition comprising a second chemiluminescent substrate capable of being activated by a second enzyme to produce a second chemiluminescent signal, and detecting the second chemiluminescent signal on the surface layer of the solid support (see in particular column 6, lines 17-24, 41-45 and 60-67; and column 7, lines 1-46; column 10, lines 59-67; and column 11, lines 1-44).

Akhavan-Tafti '979 fails to specifically teach a method wherein a plurality of probes is disposed on the surface layer at a density of at least 50 or at least 100 discrete areas per cm^2. The reference also fails to specifically teach that both the first and second chemiluminescent substrates are 1,2-dioxetane substrates.

The reference also fails to specifically teach a method wherein the first substrate is a 1,2-dioxetane substrate and the second is an acridan, enol phosphate, or luminol substrate. Akhavan-Tafti '979 teaches that the first chemiluminescent substrate used in a sequential detection method must be capable of being inhibited, and that the use of a horseradish peroxidase substrate such as an acridan compound is preferred as the first chemiluminescent substrate because of the ability to inhibit peroxidase activity (column 7, lines 65-67 to column 8, lines 1-23).

As noted above with respect to claim 1, Akhavan-Tafti et al. teach chemiluminescent detection of DNA in low- and medium-density arrays of 100 spots per cm^2 (p. 2065, right column, paragraph 4). Akhavan-Tafti et al. further teach that such arrays are useful in high-throughput analysis of gene mutations and gene expression (p. 2065, right column, paragraph 1)

and can be combined with chemiluminescent analysis with no expensive instrumentation (p. 2066, right column, last paragraph).

Therefore, as previously discussed above with respect to claim 1, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ the method of sequentially detecting chemiluminescent emissions of Akhavan-Tafti '979 using arrays with a plurality of probes disposed on a surface layer at a density of at least 50 or 100 discrete areas per cm^2 as taught by Akhavan-Tafti et al. in order to allow high-throughput analysis of gene mutations and expression. One would have had reasonable expectation of success in combining the array of Akhavan-Tafti et al. with the sequential chemiluminescent detection method of Akhavan-Tafti '979 because Akhavan-Tafti et al. established that chemiluminescent detection was feasible with array formats. One would also have a reasonable expectation of success because the sequential detection method of Akhavan-Tafti '979 involves detection of chemiluminescent emissions on a nylon membrane, which is the same material used as the solid support in Akhavan-Tafti '979.

Greene et al. teach inhibitors of the enzyme alkaline phosphatase, which include inorganic phosphate, chelating agents, and amino acids (column 6, lines 9-29), in the context of enzyme-based detection methods using alkaline phosphatase, horseradish peroxidase, and other enzymes (column 6, lines 30-37 and column 10, lines 19-30).

Therefore, it would have been further obvious to one of ordinary skill in the art at the time of the invention to use a horseradish peroxidase substrate (such as an acridan) in the method of Akhavan-Tafti '979 and Akhavan-Tafti et al. as the second, rather than the first substrate, and to use a 1,2-dioxetane substrate capable of being activated by alkaline phosphatase as the first,

rather than the second substrate, for the same purpose in generating chemiluminescent signals because Greene et al. teaches that alkaline phosphatase, like horseradish peroxidase, may also be readily inhibited in assays that employ this enzyme, such as those of Akhavan-Tafti '979 and Akhavan-Tafti et al. One would have a reasonable expectation of success in using alkaline-phosphatase-cleavable 1,2-dioxetanes as the first substrate in the method of Akhavan-Tafti '979 and Akhavan-Tafti et al. because Greene et al. teach that alkaline phosphtase is capable of being inhibited, which is in accord with the teachings of Akhavan-Tafti '979, which directs the skilled artisan to employ a first chemiluminescent substrate that is capable of being inhibited.

30. Claims 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akhavan-Tafti '979 and Akhavan-Tafti et al. and Bronstein et al. as applied to claim 1 above, and further in view of Akhavan-Tafti (US Patent No. 5,523,212).

Akhavan-Tafti '979 and Akhavan-Tafti et al. teach preferred formulations for chemiluminescence but fails to specifically teach additives and counterions.

Akhavan-Tafti '212 teach chemiluminescent formulations for the detection of biological molecules that comprise enhancers and additives such as β–cyclodextrin, polyols, and sulfate (column 15, lines 45-59; column 16, lines 1-21; and Examples 13 and 20), and it is further taught that useful levels of light intensity compared to reagent background are obtained with reagents that incorporate dextran sulfate and β–cyclodextrin (Example 20).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ dextran sulfate and β-cyclodextrin, as taught by Akhavan-Tafti '212 in the chemiluminescent formulations comprising enhancers in the method of Akhavan-Tafti '979,

Akhavan-Tafti et al., and Bronstein et al. in order to achieve useful light intensity over background in methods for chemiluminescent detection of biological molecules, such as those of Akhavan-Tafti '979 and Akhavan-Tafti et al.

Response to Arguments

31. Applicant's arguments filed 1/17/2007 have been fully considered.

32. With respect to the rejections of claims 24 and 30 under 35 USC 112, 1st paragraph (new matter), Applicant's arguments (see p. 11, first paragraph) have been considered but are moot in light of the new grounds of rejection set forth above.

33. With respect to the rejections of claims 13-19, 29-31, and 37-38 under 112, 2nd paragraph (see above and the previous Office action at p. 8, item 15), Applicant's reply does not specifically address the rejection (see reply, p. 11, the second paragraph). The rejection is maintained for reasons of record.

34. With respect to the rejections of claims 1, 3-5, 7, 9, 13-15, 21, 25, 27-39, 31-32, 40-41 and 44 under 35 USC 103(a) as being unpatentable over Akhavan-Tafti '979 in view of Akhavan-Tafti, Applicant argues (see p. 12-13) that the Akhavan-Tafti reference fails to specifically teach 1,2-dioxetane substrates (see especially p. 12).

This argument is not found persuasive because it amounts to a piecemeal analysis of the references. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the Akhavan-Tafti reference was relied upon not for teaching 1,2-

dioxetane substrates but for its teaching of chemiluminescent detection in medium-density arrays of at least 50-100 discrete areas per cm^2. Rather, the Akhavan-Tafti '979 reference teaches 1,2-dioxetanes substrates, for example at column 8, line 65 to column 10, line 14.

Thus, the fact that the secondary reference Akhavan-Tafti fails to specifically teach 1,2-dioxetane substrates is not persuasive to establish unexpected results since such substrates are taught in the primary reference.

Applicant further argues that there is objective evidence of non-obviousness and points to the Declaration under 35 USC 1.132 previously submitted on 5/9/2006. However, the Declaration is ineffective to demonstrate unexpected results because a comparison of the closest prior art relied upon has not been made with the claimed invention (see also the previous Office action at p. 35). Applicant has not established a nexus between the merits of the invention and the asserted secondary considerations of unexpected results, because the features asserted to be responsible for the unexpected results are not related to those features that distinguish the claimed invention over the closest prior art of record.

Specifically, Applicant argues that the Declaration provides evidence of significant improvements in array performance by using (1) an onium polymer or copolymer chemiluminescent enhancing material and a (2) chemiluminescent 1,2-dioxetane substrate in a microarray format on a two-dimensional support (see p. 12-13).

However, the primary reference relied upon, Akhavan-Tafti '979, discloses the use of (1) 1,2-dioxetane substrates such as Lumigen PPD (columns 8-10) and also discloses (2) chemiluminescent quantum yield enhancing materials that are onium polymers, e.g. polymeric onium salts (column 10). The Declaration is therefore ineffective to establish unexpected results

because it does not establish a nexus between the asserted improved performance and the differences between the claimed invention and the closest prior art.

In addition, the Declaration is ineffective because the scope of the showing must be commensurate with the scope of the claims. *In re Coleman,* 205 USPQ 1172; *In re Greenfield,* 197 USPQ 227; *In re Lindener,* 173 USPQ 356; *In re Payne,* 203 USPQ 245. The Declaration relates to the use of a single 1,2-dioxetane substrate (TFE-CDP-Star®) (and a single enzyme conjugate), while the claims are drawn to the use of two 1,2-dioxetane substrates. Further, the Declaration is not commensurate with the scope of the claims because the claims are drawn to any two 1,2-dioxetane substrates, while the Declaration pertains only to TFE-CDP-Star®.

In addition, the Declaration is not commensurate with the scope of the claims because the claims are drawn to any onium polymer or onium copolymer as the quantum yield enhancing material, while the Declaration pertains only to the use of "TPQ polymer enhancer" (see p. 2 of the Declaration at item 7), which does not even appear to be an onium polymer or copolymer. The Declaration does not specifically identify this material; however, the prior art teaches that "TPQ" stands for 1,3,4-tris[3-phenyl-6-trifluoromethyl]quinoxaline-2-yl)benzene (see Woo et al., US 20020061419 A1, see [0065]). Since "TPQ" itself lacks any "onium" groups or substituents, the use of "TPQ polymer" in the experiment of the Declaration fails support Applicant's arguments (see p. 13) that the Declaration provides evidence of unexpected results associated with the use of onium polymers or copolymers since the Declaration does not describe the use of any "onium" polymers or copolymers. Accordingly, the Declaration is also incommensurate with the scope of the claims since there is nothing of record to show that the "TPQ polymer enhancer" used in the experiment of the Declaration would even represent a

species reading on the claimed genus of a composition comprising an onium polymer or an onium copolymer. It is noted that even if the "TPQ polymer enhancer" of the Declaration were to be established by supporting documentation to be an example of an onium polymer or an onium copolymer, such evidence would be insufficient to establish unexpected results since onium polymers are also taught in the primary reference. Applicant has not established a nexus between the merits of the invention and the asserted secondary considerations of unexpected results, because the features asserted to be responsible for the unexpected results are not related to those features that distinguish the claimed invention over the closest prior art of record.

As previously noted, the Declaration also pertains only to solid supports that are *film*, while the claims are broadly drawn to *two-dimensional solid supports* (see the previous Office action at p. 36). The Declaration also describes *overcoating* a high-density array with the TPQ polymer, while the claims relate only to contacting the chemiluminescent substrate *in the presence of* an onium polymer or copolymer, which would include various means of simultaneous contact other than overcoating the support itself.

For all of these reasons, the Declaration is insufficient to demonstrate unexpected results there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716.

Finally, as noted in the previous Office action (see p. 36), the use of onium polymers was known in the art to improve the signal/background ratio of enzymatically performed chemiluminescence (see for example Akhavan-Tafti '979 at column 10, lines 26-36). Therefore, the Declaration is ineffective to establish unexpected results due to the use of such onium polymers since such compounds would in fact be *expected* to improve the chemiluminescent

signal. Consequently, the Declaration is insufficient to demonstrate unexpected results because the property or result must actually be unexpected. *In re Skoll,* 187 USPQ 481, 484; *In re Coleman,* 205 USPQ 1172.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Conclusion

35. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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